

Suggestion to hire attorney section # 4 – The services of a professional patent attorney were obtained briefly. His fees, however, became so high that it was not sensible to continue with him.

Claim objections section # 5 – Claims 5-7 were objected to as being in improper form. This was corrected by rewriting the claims.

Claim rejection section # 6 and 7 – Objection that claim 7 did not properly describe method for use. This was corrected. Current claim should comply. Contains example and describes how to use it.

Claim rejection section # 8 and 9 – Objection that claims 1-7 were indefinite for failing to particularly point out and distinctly claim the subject matter. This was corrected. All seven claims were rewritten to comply.

Claim rejection section # 10 – Objection that it was not clear whether claim 1 is directed at a method. It is directed at a method. Examiners suggestion for clarifying this was taken.

Claim rejection section # 11 – Objection that the metes and bounds of claim 1 were not clear. Removed reference to “similar modifications can be inferred”. Instead included specific tables of data that were determined during the work which led to this invention. Entire claim was modified to comply.

Claim rejection section # 12 – Objection that reference to “peptide-like, hormone-like, and protein-like” in claim 1 was not a clear definition. This phrase (which is specialized scientific terminology) was changed to a more specific description.

Claim rejection section # 13 – Objection that reference “to the right of the amide” in claim 1 was not a clear definition. This phrase (which again is specialized scientific terminology) was changed to carboxyl-side which is more exact. Entire claim was clarified.

Claim rejection section # 14 – Asks what effects are known of modifications in claim 1. These effects are known from data taken in the course of the work which led to the patent. Claim 1 was rewritten with examples to answer this question and comply.

Claim rejection section # 15 – Objection that claims 1-7 omit essential steps. All claims were modified with specific examples where necessary to correct this problem. In claims 1-4 the outcome can be predicted as shown by the examples now present in the claims. In claims 1-7 method allows prediction of results. That is the purpose of the method. Results can be verified by many different experimental procedures. Many of these are referenced in the application, particularly on the enclosed CD of book – *Molecular Clocks*.

Claim rejection section # 16 – Question about definition of the term "near vicinity" in claim 4. The term "near vicinity" would be understood by those skilled in the art of and actually using this method. It refers to atoms that are within a certain nearby but varying proximity to the amide in such a way that they can effect the reaction. The method sets out precisely what this means in each case. An example of how this is done has been inserted in claim 4 and the confusing terminology has been modified to improve this.

Claim rejection section # 17 – Objection that claim 7 is not clear in what method/process is intended to be encompassed and steps showing how to apply to use it needed. This claim was updated with an example showing how to use the method.

Claim rejection section # 18 and 19 – Objection that no utility is established in claim 7. This has been corrected showing exactly how to use this method to change deamidation rates to any programmed time interval.

Claim rejection section # 20 and 21 – This rejection to claims 1-6 was based on prior art described in the Wright reference. This was also specifically mentioned in your letter of February 24<sup>th</sup>, 2006. That deamidation is sequence dependent and the mechanism of reaction, has been known for a long time before the Wright reference. Some data on deamidation rates of a few sequences had been measured.

What is unique and was discovered in this invention was exactly how this sequence dependence functioned. The Wright reference describes part of the basic mechanism for peptides, but there is not enough data to predict deamidation rates. Other than the knowledge that large nearby groups and inhibitory structures tended to slow deamidation rates, nothing to determine these actual rates – the focus of this application – was described. It was not possible before this invention to effectively design a peptide with a given deamidation rate. For proteins, the situation was even worse, so the only way to determine a protein or even a peptide deamidation rate was through direct and laborious measurement of each individual rate. If an experimenter wished to change the rate through modification of sequence or structure, it would be extremely difficult trying all sorts of possibilities.

Now, with the procedures described in this patent, the situation has been entirely changed. The extensive work and insights which went into measuring and systematizing peptide deamidation rates (for example see Tables 1 and 2 in the application) allows a researcher to pick any sequence and know what the deamidation rate will be, or to pick a needed rate and select from a variety of available sequences.

For protein work, the methods, approach to the methods, and techniques for determining deamidation rates as described in this application are entirely unique and novel. Nothing along these lines has been attempted before. The technique was so successful, however, that it has been applied by me to the entire protein databank and the deamidation rate of every asparagine in every protein for which a three

dimensional structure was available has been computed. This data is updated periodically and is available at [www.deamidation.org](http://www.deamidation.org).

Rates of amide deamidation in new proteins can be computed with this method. Design of proteins with specific deamidation rates can be done. The methods may also be applied to molecules that have similar structures to peptides and proteins.

The methods developed in this patent are extremely important and have wide spread applications. The Wright reference describes some preliminary work done by others on this subject. This application is intended to cover, however, controlled calculation and directed modifications of deamidation rates in ways that are new and not anticipatable from the Wright reference.

Thank you very much for your time and attention to this response.

Best Regards,

Noah Robinson

A handwritten signature in black ink, appearing to read "Noah Robinson", written in a cursive style.



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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
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EXAMINER
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ART UNIT	PAPER
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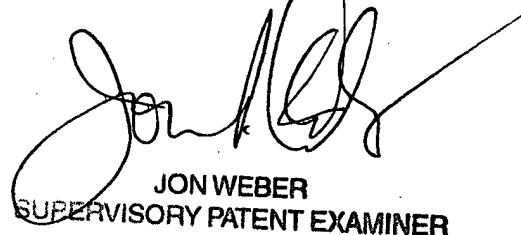
Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

The reply filed on October 28, 2005 is not fully responsive to the prior Office Action because of the following omission(s) or matter(s): The Amendment filed November 25, 2005 is non-responsive because the reply does not distinctly and specifically point out the supposed errors in the examiner's action. See 37 CFR 1.111. Since the above-mentioned reply appears to be *bona fide*, applicant is given **ONE (1) MONTH or THIRTY (30) DAYS** from the mailing date of this notice, whichever is longer, within which to supply the omission or correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a).

Applicant is referred to 37 CFR § 1.111 Reply by applicant or patent owner to a non-final Office action.

(b) In order to be entitled to reconsideration or further examination, the applicant or patent owner must reply to the Office action. The reply by the applicant or patent owner must be reduced to a writing which distinctly and specifically points out the supposed errors in the examiner's action and must reply to every ground of objection and rejection in the prior Office action. The reply must present arguments pointing out the specific distinctions believed to render the claims, including any newly presented claims, patentable over any applied references. If the reply is with respect to an application, a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated. The applicant's or patent owner's reply must appear throughout to be a bona fide attempt to advance the application or the reexamination proceeding to final action. A general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references does not comply with the requirements of this section. For example, when responding to the examiner's rejection of the Office action mailed 8/11/2004, describe why the Wright reference does not describe the method being claimed. Discuss what aspects are novel or non-obvious when comparing the claim with the prior art Wright reference.

  
JON WEBER  
SUPERVISORY PATENT EXAMINER